REMARKS

Claims 2-5 and 7 are pending in the present application and are rejected.

Applicants' Response to Claim Rejections under 35 U.S.C. §112

Claims 2-5 and 7 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

It is the position of the Office Action that the specification does not describe or discuss that "beads-ID recognizing address linkers are specific to each of said beads." The Office Action notes that the specification instead states "address linker 3 (address-judging antigen or address-judging antibody) for recognizing specific beads number ID is fixed on the surface of the beads 1." This is a quotation of the passage at page 3, lines 23-25. In support of the position that the specification does not support the recited subject matter, the Office Action states that in Figure 2, all of the addressing probe proteins are illustrated identically.

In response, Applicants herein amend claim 7 in order to clarify the claimed subject matter. Applicants herein amend claim 7 in order to recite that each bead includes one of a plurality of beads-ID. Further, each beads-ID recognizing address linker 3 is specific to one of a plurality of beads-ID. In other words, if the system included four beads (for the sake of simplicity in explanation), the following chart summarizes the relationship between the beads, beads-ID and beads-ID recognizing address linker, and is fully supported:

Bead 1	**Beads ID**	**Beads ID-recognizing address linker 3**
1	aaa	AAA
2	aaa	AAA
3	bbb	BBB
4	bbb	BBB

Thus, a bead-ID recognizing address linker 3 is specific to *each beads-ID*. This permits multiple beads to be assigned the same beads-ID. In other words, each type of bead has a beads-ID for discriminating each type thereof. If the probes of 100 sites are spotted on the substrate, 100 *types of* beads exist. The quantity of *each type of* bead existing in the solution would then be several tens of thousands. Thus, for example, if the number of beads existing in the solution is 100,000,000, the number of beads-ID could be 100, and the beads having the same beads-ID would each exist in several tens of thousands. Applicants respectfully submit that this more clearly recites the disclosed subject matter, and is fully supported by the specification.

Additionally, Applicants respectfully submit that although the Office Action notes that in Figure 2A all of the addressing probe proteins 12 appear to be illustrated identically, this is not relevant to the claim feature in issue. The recited subject matter relates to the specificity between the address linker 3 and the beads 1. As described elsewhere in the specification, the interaction between address linker 3 and addressing probe proteins 12 are an antigen/antibody reaction. In view of the fact that the recited subject matter regards the specificity of address linker 3 for the

beads 1, it is unclear why the Office Action refers to the addressing probe protein 12, which interacts with the address linker 3. Clarification is respectfully requested.

As discussed above, Applicants respectfully submit that the passage at page 3, lines 23-25 fully supports the present claims. If the beads-ID recognizing address linkers 3 were not specific to each of the beads-ID, it would be impossible to recognize a specific beads number ID. Therefore, it is clear that the beads-ID recognizing address linkers 3 are specific to each of the beads-ID. Favorable reconsideration is respectfully requested.

Applicants' Response to Claim Rejections under 35 U.S.C. §103

Claims 2, 4, 5 and 7 were rejected under 35 U.S.C. §103(a) as being unpatentable over Balasubramanian et al. (WO 00/06770) in view of Chee et al. (U.S. Patent No. 6,858,394).

It is the position of the Office Action that Balasubramanian discloses the invention as claimed, with the exception of teaching spatially addressing the beads by an antigen/antibody reaction. The Office Action relies on Chee to provide this teaching, stating that Chee illustrates the addressability of specific substrates using analyte binding on a second substrate. It is noted that the Chee reference presently cited is different from the Chee reference cited in the October 31, 2006 Office Action (Chee '027).

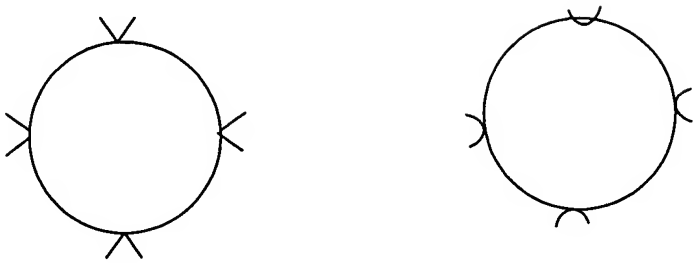
As discussed in Applicants' previous comments, Balasubramanian is directed at arrayed biomolecules and their use in sequencing. As illustrated in Figure 2, Balasubramanian contemplates an array in which a microsphere 1 is bound to a substrate by an association between

streptavidin 2 formed on the microsphere 1 and biotin 3 formed on the substrate. Additionally, a fluorescently labeled polynucleotide 4 is attached to the microsphere bead 1 by an association between streptavidin 2 formed on the microsphere and biotin 3 bound to the end of the polynucleotide.

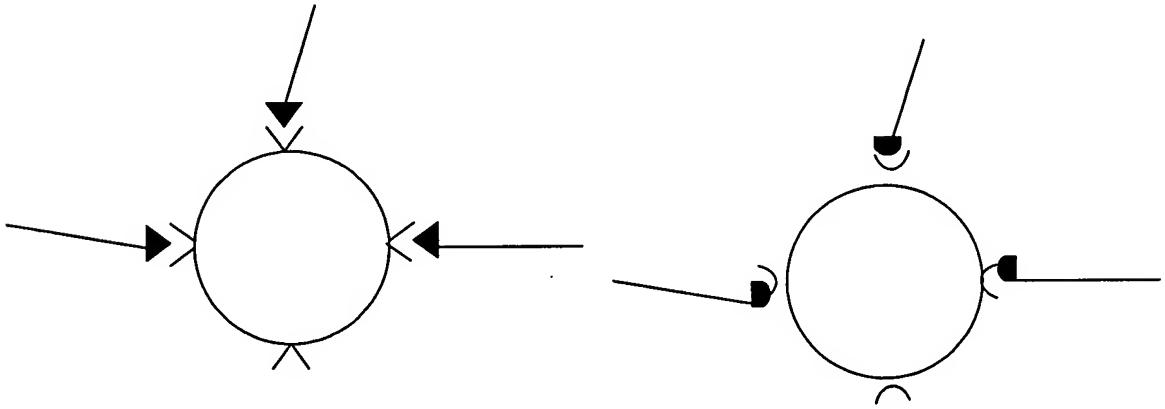
Chee is directed at composite arrays utilizing microspheres, as generally illustrated in Figures 1A, 1C and 1D. These microspheres are bound to a substrate in an array. The microspheres may be bound to the substrate randomly or non-randomly. These beads may have a bioactive agent such as DNA or RNA bound to them. The Office Action refers to Figure 1F, which is alleged to illustrate the use of binding functionalities to "target" first substrates 10 to locations on the second substrate 40.

The Office Action states that it would have been obvious "to have modified the protein interaction of Balasubramanian with the specific antibody/antigen interaction taught by Chee." It appears that by this, the Office Action alleges that it would have been obvious to substitute the avidin/streptavidin reaction with a specific antibody/antigen interaction. In response, Applicants respectfully submit that one having ordinary skill in the art would not have been prompted to modify Balasubramanian as proposed by the Office Action.

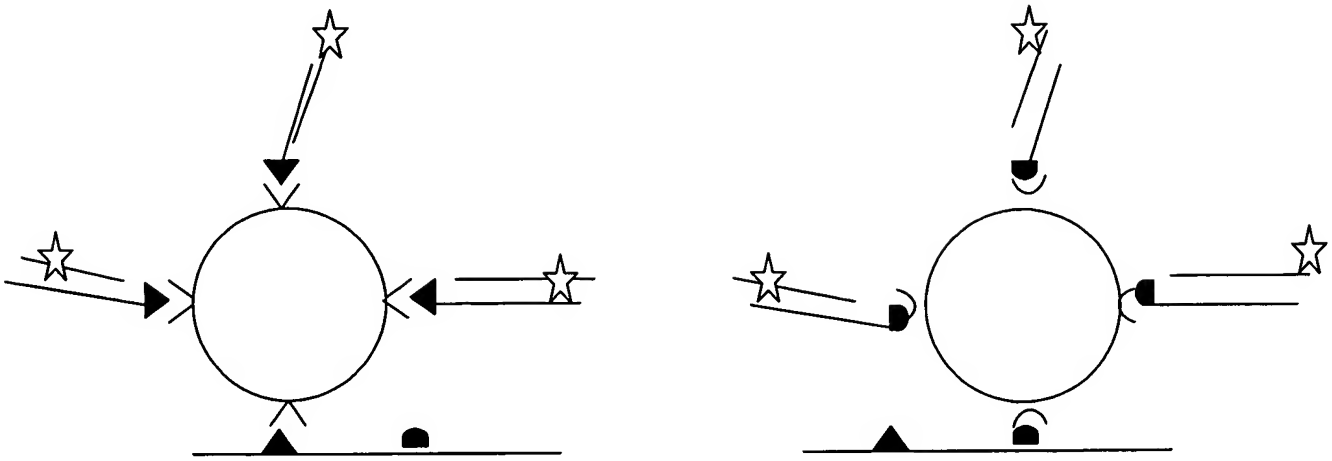
It appears that the proposed modification of Balasubramanian would take the form as illustrated in the crude drawings below. First, half of an antigen/antibody pair would be deposited on the beads, with each half of an antigen/antibody pair being specific to a bead.



Next, single-stranded-DNA having the other half of the antigen/antibody pair would be bound to the microspheres by the corresponding antigen/antibody reaction:



Next, the probe and target would be hybridized, the target having a fluorescent tag. Finally, the combination of the microsphere, probe and target would be coupled to the substrate via the antigen/antibody binding. If the antigen/antibody halves on the microspheres were specific to each microsphere, then multiple different antigen/antibody halves would have to be deposited on the substrate in order for the assay to be viable.



However, Applicants respectfully submit that one having ordinary skill in the art would not have been prompted to modify Balasubramanian in this manner. The proposed modification would drastically alter the method of Balasubramanian. As discussed at page 14, line 29 to page 15, line 6, the application of the biotin and avidin is done in a non-specific manner. With regard to the substrate, an aliquot of biotin-BSA is deposited and incubated on a substrate. It would not have been obvious to modify the substrate of Balasubramanian such that individual sites were applied with halves of different antigen/antibody pairs. This would greatly increase the cost and time involved in the preparation of the substrate.

Similarly, the proposed modification would drastically alter the preparation of the microspheres of Balasubramanian. In Balasubramanian, non-fluorescent streptavidin functionalized polystyrene latex microspheres of a diameter of 500 nm (made by Polysciences, Inc.) are used. Pending claim 7 requires that the beads-ID recognizing address linkers are specific to each beads-ID. Thus, in order to arrive at the proposed modification, each antigen/antibody half must be specific to a single beads-ID. Accordingly, the proposed

modification would require many different types of beads, rather than a single type of bead. This would dramatically increase the cost and complexity of the system of Balasubramanian.

Furthermore, the proposed modification of Balasubramanian would be undesirable for another reason. As discussed above, in Balasubramanian, the probe DNA is attached to the microspheres by avidin/streptavidin interactions. Thus, all probe DNA is biotinated. However, if Balasubramanian were modified as proposed by the Office Action, probe DNA would have to be prepared having different antigens/antibodies bound to each probe. Accordingly, this would greatly increase the complexity, preparation time and expense of the system of Balasubramanian.

Additionally, Applicants note that the claimed embodiment is premised on the fact that the number of configurations of antibody/antigen is the same as the number of sites. Therefore, the number of beads-ID and the number of combinations of antigen/antibody pairs are both the same number as the number of sites. Therefore, Applicants respectfully submit that, for at least the reasons discussed above, it would not have been obvious to modify Balasubramanian as suggested by the Office Action. Favorable reconsideration is respectfully requested.

Claim 3 was rejected under 35 U.S.C. §103(a) as being unpatentable over Balasubramanian in view of Chee, and in further view of Collier et al. (U.S. Patent No. 5,985,548).

It is the position of the Office Action that the combination of Balasubramanian and Chee discloses the invention as claimed, with the exception of stirring beads. The Office Action relies on Collier to provide this teaching.

In response, Applicants respectfully submit that Collier does not make up for the teachings that Balasubramanian and Chee lack, as discussed above. Accordingly, Applicants respectfully submit that claim 3 is patentable at least due to its dependency on claim 1, which Applicants submit is patentable for at least the reasons discussed above. Favorable reconsideration is respectfully requested.

For at least the foregoing reasons, the claimed invention distinguishes over the cited art and defines patentable subject matter. Favorable reconsideration is earnestly solicited.

Should the Examiner deem that any further action by applicants would be desirable to place the application in condition for allowance, the Examiner is encouraged to telephone applicants' undersigned attorney.

If this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. The fees for such an extension or any other fees that may be due with respect to this paper may be charged to Deposit Account No. 50-2866.

Respectfully submitted,

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